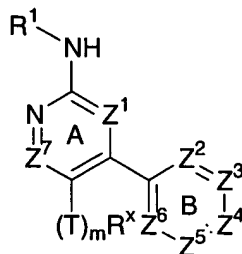


## CLAIMS

1. A compound of formula I:



**I**

or a pharmaceutically acceptable salt thereof,

wherein:

$R^1$  is  $Q-Ar^1$ ,

wherein Q is a  $C_{1-2}$  alkylidene chain wherein one methylene unit of Q is optionally replaced by O, NR, NRCO, NRCONR, NR $CO_2$ , CO,  $CO_2$ , CONR, OC(O)NR,  $SO_2$ ,  $SO_2NR$ ,  $NRSO_2$ ,  $NRSO_2NR$ , C(O)C(O), or C(O)CH $_2$ C(O);

$Ar^1$  is a 5-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein  $Ar^1$  is optionally substituted with q independent occurrences of  $Z-R^Z$ ; wherein q is 0-5, Z is a bond or is a  $C_1-C_6$  alkylidene chain wherein up to two non-adjacent methylene units of Z are optionally and independently replaced by CO,  $CO_2$ , COCO, CONR, OCONR, NRNR, NRNRCO, NRCO,  $NRCO_2$ , NRCONR, SO,  $SO_2$ ,  $NRSO_2$ ,  $SO_2NR$ ,  $NRSO_2NR$ , O, S, or NR; and each occurrence of  $R^Z$  is independently selected from  $R'$ , halogen,  $NO_2$ , CN,  $OR'$ ,  $SR'$ ,  $N(R')_2$ ,  $NR'COR'$ ,  $NR'CON(R')_2$ ,  $NR'CO_2R'$ ,  $COR'$ ,  $CO_2R'$ ,  $OCOR'$ ,  $CON(R')_2$ ,  $OCON(R')_2$ ,  $SOR'$ ,  $SO_2R'$ ,  $SO_2N(R')_2$ ,  $NR'SO_2R'$ ,  $NR'SO_2N(R')_2$ ,  $COCOR'$ , or  $COCH_2COR'$ ;

each occurrence of R is independently hydrogen or an optionally substituted  $C_{1-6}$  aliphatic group; and each occurrence of  $R'$  is independently hydrogen or an optionally substituted  $C_{1-6}$

aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or R and R', two occurrences of R, or two occurrences of R', are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Z<sup>1</sup> is N or CH;

Z<sup>7</sup> is N or C(U)<sub>n</sub>R<sup>Y</sup>;

T and U are each independently a bond or a saturated or unsaturated C<sub>1-6</sub> alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by CO, CO<sub>2</sub>, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO<sub>2</sub>, NRCONR, SO, SO<sub>2</sub>, NRSO<sub>2</sub>, SO<sub>2</sub>NR, NRSO<sub>2</sub>NR, O, S, or NR;

m and n are each independently 0 or 1;

R<sup>X</sup> and R<sup>Y</sup> are each independently selected from R or Ar<sup>1</sup>;

Z<sup>2</sup> is N or CR<sup>2</sup>; Z<sup>3</sup> is N or CR<sup>3</sup>; Z<sup>4</sup> is N or CR<sup>4</sup>; Z<sup>5</sup> is N or CR<sup>5</sup>; and Z<sup>6</sup> is N or CR<sup>6</sup>, wherein each occurrence of R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> or R<sup>6</sup> is independently R<sup>U</sup> or (V)<sub>p</sub>R<sup>V</sup>, provided that a) no more than three of Z<sup>2</sup>, Z<sup>3</sup>, Z<sup>4</sup>, Z<sup>5</sup> or Z<sup>6</sup> is N, and b) at least one of Z<sup>3</sup>, Z<sup>4</sup> or Z<sup>5</sup> is CR<sup>3</sup>, CR<sup>4</sup>, or CR<sup>5</sup>, respectively, and at least one of R<sup>3</sup>, R<sup>4</sup>, or R<sup>5</sup> is R<sup>U</sup>,

each occurrence of R<sup>U</sup> is NRCOR<sup>7</sup>, CONR(R<sup>7</sup>), SO<sub>2</sub>NR(R<sup>7</sup>), NRSO<sub>2</sub>R<sup>7</sup>, NRCONR(R<sup>7</sup>), NRSO<sub>2</sub>NR(R<sup>7</sup>), or CONRNR(R<sup>7</sup>), wherein R<sup>7</sup> is (CH<sub>2</sub>)<sub>t</sub>-Y-R<sup>8</sup>, and t is 0, 1, or 2, Y is a bond or is O, S, NR<sup>9</sup>, -OCH<sub>2</sub>-, -SCH<sub>2</sub>-, -NR<sup>9</sup>CH<sub>2</sub>-, O(CH<sub>2</sub>)<sub>2</sub>-, -S(CH<sub>2</sub>)<sub>2</sub>-, or -NR<sup>9</sup>(CH<sub>2</sub>)<sub>2</sub>-, and R<sup>8</sup> is Ar<sup>2</sup>, or R<sup>8</sup> and R<sup>9</sup>, taken together with the nitrogen atom, form an optionally substituted 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each occurrence of V is a bond or a saturated or unsaturated C<sub>1-6</sub> alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by CO, CO<sub>2</sub>, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO<sub>2</sub>, NRCONR, SO, SO<sub>2</sub>, NRSO<sub>2</sub>, SO<sub>2</sub>NR, NRSO<sub>2</sub>NR, O, S, or NR;

each occurrence of p is 0 or 1;

each occurrence of  $R^V$  is R or  $Ar^2$ ; and

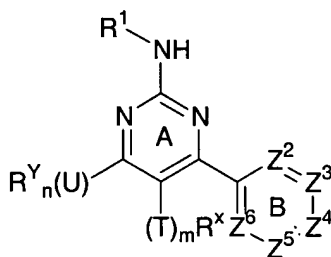
$Ar^2$  is a 5-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein  $Ar^2$  is optionally substituted with r independent occurrences of  $W-R^W$ ; wherein r is 0-3, W is a bond or is a  $C_1-C_6$  alkylidene chain wherein up to two non-adjacent methylene units of W are optionally replaced by CO,  $CO_2$ , COCO, CONR, OCONR, NRNR, NRNRCO, NRCO,  $NRCO_2$ , NRCONR, SO,  $SO_2$ ,  $NRSO_2$ ,  $SO_2NR$ ,  $NRSO_2NR$ , O, S, or NR; and each occurrence of  $R^W$  is independently selected from  $R'$ , halogen,  $NO_2$ , CN,  $OR'$ ,  $SR'$ ,  $N(R')_2$ ,  $NR'COR'$ ,  $NR'CON(R')_2$ ,  $NR'CO_2R'$ ,  $COR'$ ,  $CO_2R'$ ,  $OCOR'$ ,  $CON(R')_2$ ,  $OCON(R')_2$ ,  $SOR'$ ,  $SO_2R'$ ,  $SO_2N(R')_2$ ,  $NR'SO_2R'$ ,  $NR'SO_2N(R')_2$ ,  $COCOR'$ , or  $COCH_2COR'$ ;

provided that:

a) when  $Z^1$  is N,  $Z^7$  is CH; and ring B is phenyl and at least one of  $R^3$  or  $R^4$  is  $NHCOR^7$ , then  $R^1$  is not phenyl only substituted with two or three occurrences of  $OR'$ ; and

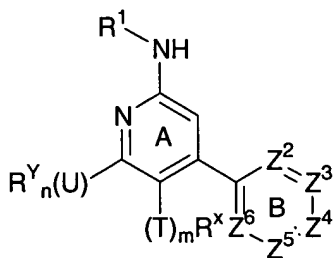
b) when  $Z^1$  is N,  $Z^7$  is CH; and ring B is phenyl and at least one of  $R^3$  or  $R^4$  is  $NHCOR^7$ ,  $SO_2R^7$ ,  $CONRR^7$ , then  $R^1$  is not phenyl only substituted with one occurrence of  $-CON(R')_2$  in the para position.

2. The compound according to claim 1, wherein  $Z^1$  is N and the compound has the structure **II**:



**II**

3. The compound of claim 1, wherein  $Z^1$  is CH and amino pyridines of general formula **III** are provided:

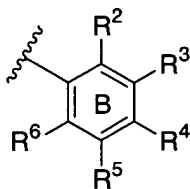


III

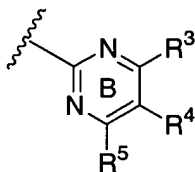
4. The compound of claim 1, wherein R<sup>1</sup> is an optionally substituted phenyl, cyclohexyl, cyclopentyl, pyridyl, morpholino, piperazinyl, or piperidinyl group
5. The compound of claim 1, wherein R<sup>1</sup> is an optionally substituted from phenyl, cyclohexyl, or pyridyl group.
6. The compound of claim 1, wherein R<sup>1</sup> is optionally substituted phenyl.
7. The compound of claim 1, wherein q is 0, 1, 2, or 3 and each independent occurrence of ZR<sup>Z</sup> is C<sub>1-4</sub>alkyl, N(R')<sub>2</sub>, OR', SR', CON(R')<sub>2</sub>, NR'COR', NR'SO<sub>2</sub>R', or SO<sub>2</sub>N(R')<sub>2</sub>.
8. The compound of claim 1, wherein q is 1 and ZR<sup>Z</sup> is -NH<sub>2</sub>, -OH, C<sub>1-4</sub>alkoxy, or -S(O)<sub>2</sub>NH<sub>2</sub>.
9. The compound of claim 1, wherein q is 1, and ZR<sup>Z</sup> is in the meta position and ZR<sup>Z</sup> is -NH<sub>2</sub>, -OH, C<sub>1-4</sub>alkoxy, or -S(O)<sub>2</sub>NH<sub>2</sub>.
10. The compound of claim 1, wherein (T)<sub>m</sub>R<sup>X</sup> and (U)<sub>n</sub>R<sup>Y</sup> are hydrogen, halogen, NO<sub>2</sub>, CN, OR, SR or N(R)<sub>2</sub>, or C<sub>1-4</sub>aliphatic optionally substituted with oxo, OR, SR, N(R)<sub>2</sub>, halogen, NO<sub>2</sub> or CN.
11. The compound of claim 1, wherein (T)<sub>m</sub>R<sup>X</sup> and (U)<sub>n</sub>R<sup>Y</sup> are each independently hydrogen, Me, OH, OMe or N(R)<sub>2</sub>.

12. The compound of claim 1, wherein  $(T)_mR^X$  and  $(U)_nR^Y$  are each hydrogen.

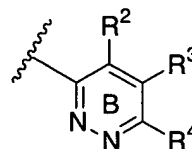
13. The compound of claim 1, wherein ring B is one of rings **i-xiv**:



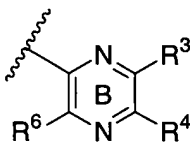
**i**



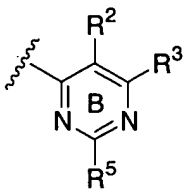
**ii**



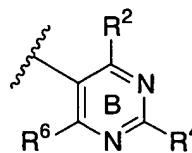
**iii**



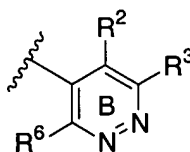
**iv**



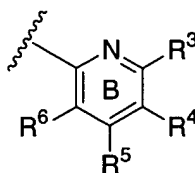
**v**



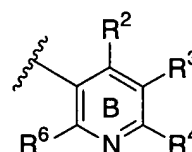
**vi**



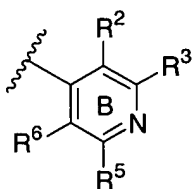
**vii**



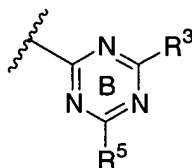
**viii**



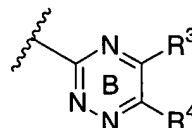
**ix**



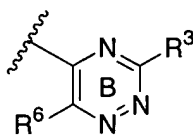
**x**



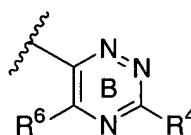
**xi**



**xii**



**xiii**



**xiv**

14. The compound of claim 1, wherein t is 0, Y is a bond, and R<sup>8</sup> is an optionally substituted aryl or heteroaryl moiety.

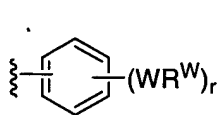
15. The compound of claim 1, wherein t is 0, Y is a bond, and R<sup>8</sup> is an optionally substituted heteroaryl moiety.

16. The compound of claim 1, wherein R<sup>7</sup> is -CH<sub>2</sub>-Y-R<sup>8</sup>, and Y is NR<sup>9</sup>, O or S, and R<sup>8</sup> is an optionally substituted aryl or heteroaryl moiety.

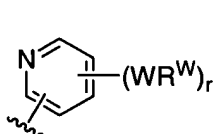
17. The compound of claim 1, wherein R<sup>7</sup> is -CH<sub>2</sub>-Y-R<sup>8</sup>, and Y is NR<sup>9</sup>, O or S, and R<sup>8</sup> is an optionally substituted aryl moiety.

18. The compound of claim 1, wherein t is 0 or 1, Y is NR<sup>9</sup>, and R<sup>8</sup> and R<sup>9</sup>, taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur.

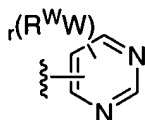
19. The compound of claim 1, wherein R<sup>8</sup> is a 5- or 6-membered aryl or heteroaryl group having one of the formulae:



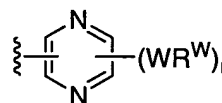
**a**



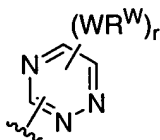
**b**



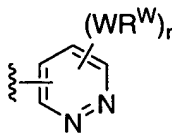
**c**



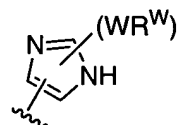
**d**



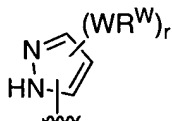
**e**



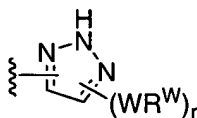
**f**



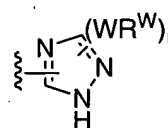
**g**



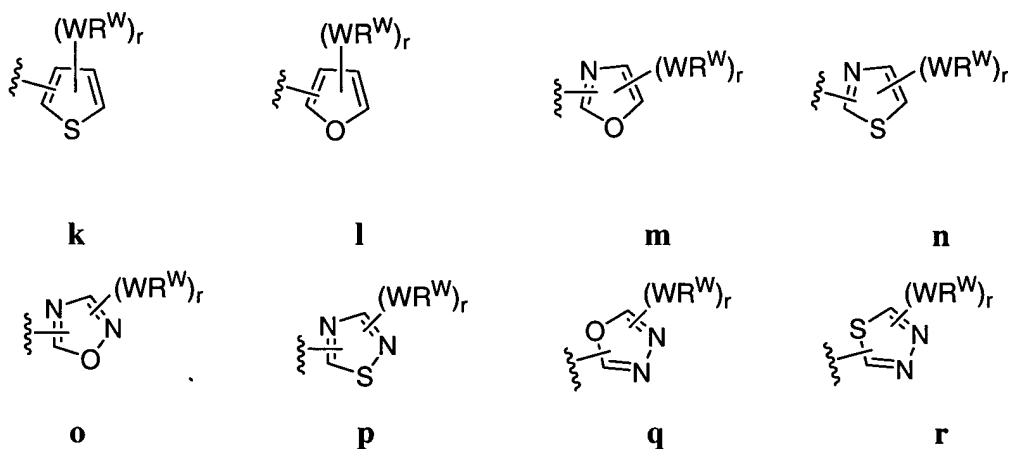
**h**



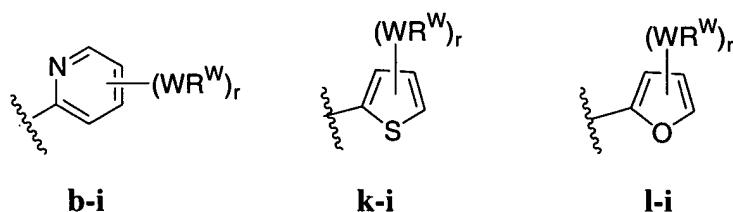
**i**



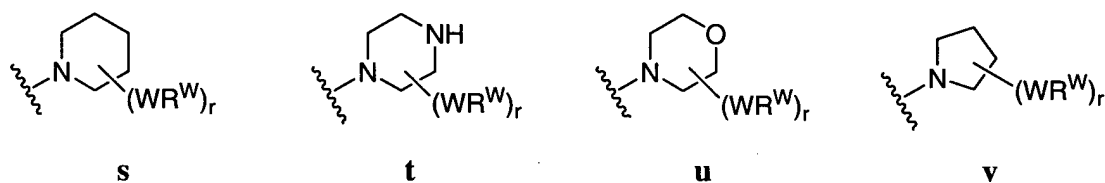
**j**



20. The compound of claim 1, wherein  $R^8$  is a 5- or 6-membered heteroaryl group having one of the formulae:



21. The compound of claim 1, wherein  $R^8$  and  $R^9$ , taken together, form a group having one of the formulae:



22. The compound of claim 1, wherein  $r$  is 0 or 1.

23. The compound of claim 19, 20, or 21, wherein  $r$  is 1, 2, or 3, and each occurrence of halogen,  $C_{1-4}$ alkyl,  $-(R)_2$ ,  $-OR$ ,  $-SR$ ,  $-SO_2N(R)_2$ ,  $-N(R)SO_2R$ ,  $-N(R)COR$ ,  $-N(R)_2$ ,  $-CH_2OR$ ,  $-CH_2N(R)_2$ , or  $-CH_2SR$ .

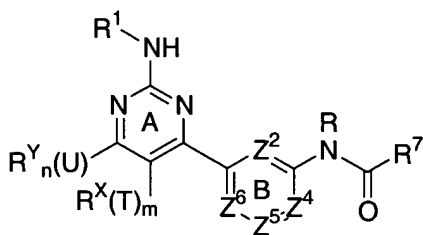
24. The compound of claim 19, 20, or 21, wherein  $t$  is 0,  $Y$  is a bond, and  $R^8$  is an optionally substituted heteroaryl moiety selected from one of groups **b** through **r**.

25. The compound of claim 24, wherein  $R^8$  is an optionally substituted heteroaryl group **b-i**, **k-i**, or **l-i**.

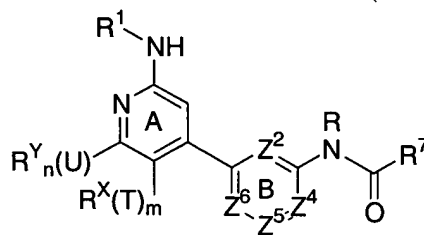
26. The compound of claim 1, wherein  $t$  is 1,  $Y$  is O, S or  $NR^9$ , and  $R^8$  is optionally substituted phenyl.

27. The compound of claim 1, wherein  $t$  is 0 or 1,  $Y$  is  $NR^9$ , and  $R^8$  and  $R^9$ , taken together form an optionally substituted group selected from **s**, **u** or **v**.

28. The compound of claim 1, wherein  $Z^3$  or  $Z^5$  is  $CR^3$  or  $CR^5$ , respectively, and  $R^3$  or  $R^5$  is  $NRC(O)R^7$ , wherein  $R^7$  is  $(CH_2)_t-Y-R^8$ , wherein  $t$  is 0, 1 or 2, wherein  $Y$  is a bond or is O, S,  $NR^9$ ,  $-OCH_2-$ ,  $-SCH_2-$ ,  $-NR^9CH_2-$ ,  $O(CH_2)_2-$ ,  $-S(CH_2)_2-$ , or  $-NR^9(CH_2)_2-$ , and wherein  $R^8$  is  $Ar^2$ , or  $R^8$  and  $R^9$ , taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur, and compounds have the formula **II-A** or **III-A**:



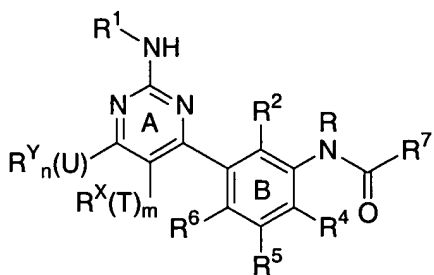
**II-A**



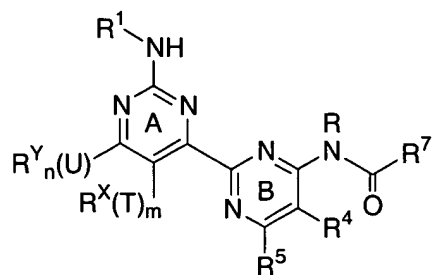
**III-A**

29. The compound of claim 28, wherein for compounds of formula **II-A** ring B is selected from **i**, **ii**, **iii**, **iv**, **v**, **vii**, **viii**, **ix**, **x**, **xi**, **xii**, or **xiii** and compounds have one of formulas **II-A-i**, **II-A-ii**, **II-A-iii**, **II-A-iv**, **II-A-v**, **II-A-vii**, **II-A-viii**, **II-A-ix**, **II-A-x**, **II-A-xi**, **II-A-xii**, or **II-A-xiii**:

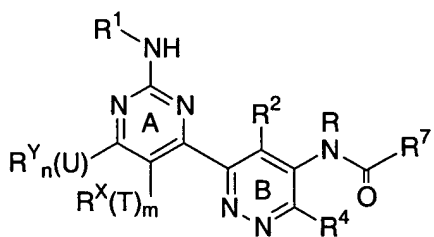




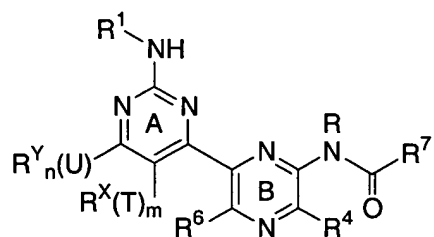
**II-A-i**



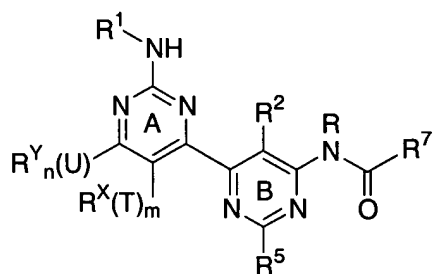
**II-A-ii**



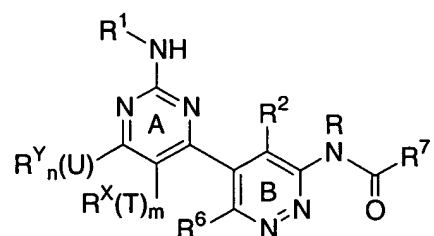
**II-A-iii**



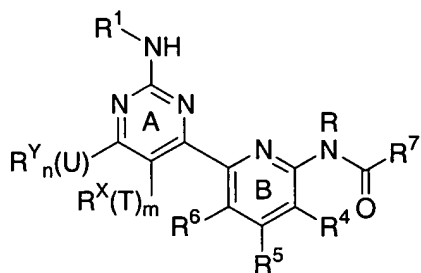
**II-A-iv**



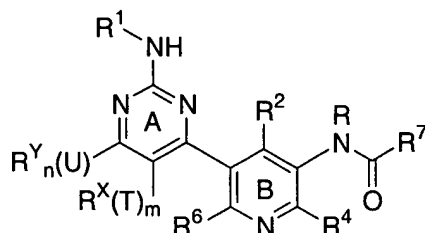
**II-A-v**



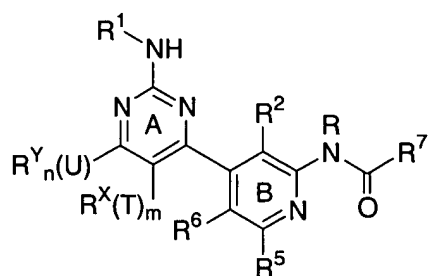
**II-A-vii**



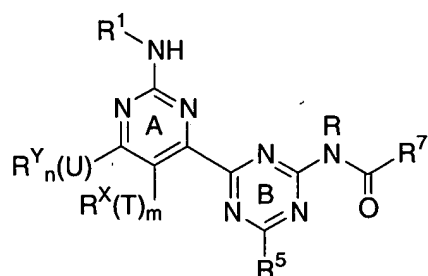
**II-A-viii**



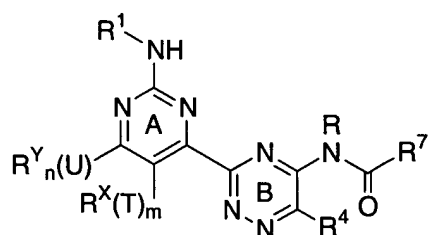
**II-A-ix**



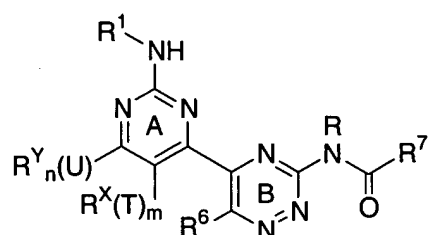
**II-A-x**



**II-A-xi**

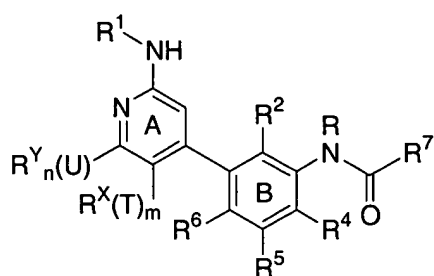


**II-A-xii**

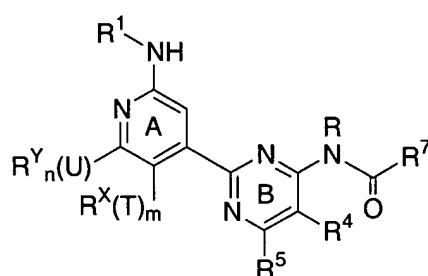


**II-A-xiii**

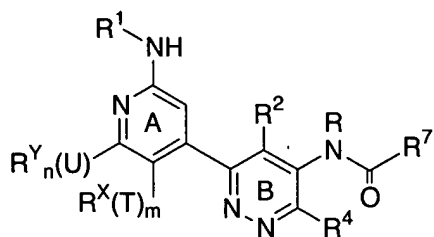
30. The compound of claim 28, wherein for compounds of formula **III-A** ring B is selected from one of **i**, **ii**, **iii**, **iv**, **v**, **vii**, **viii**, **ix**, **x**, **xi**, **xii**, or **xiii** and compounds have one of formulas **III-A-i**, **III-A-ii**, **III-A-iii**, **III-A-iv**, **III-A-v**, **III-A-vii**, **III-A-viii**, **III-A-ix**, **III-A-x**, **III-A-xi**, **III-A-xii**, or **III-A-xiii**:



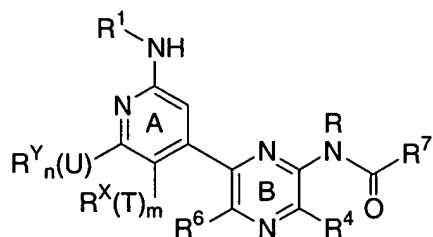
**III-A-i**



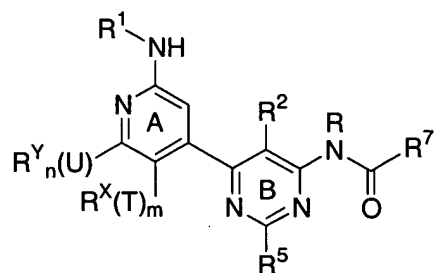
**III-A-ii**



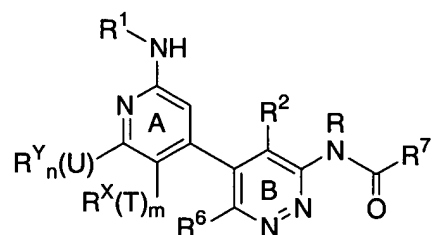
**III-A-iii**



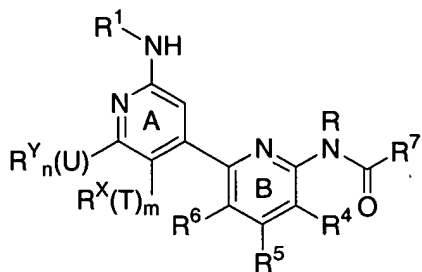
**III-A-iv**



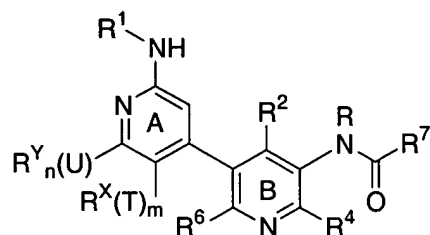
**III-A-v**



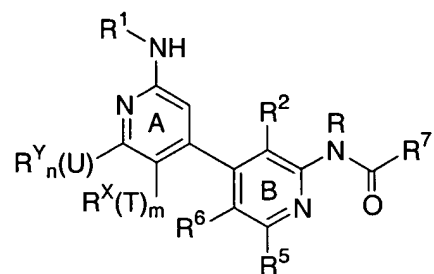
**III-A-vii**



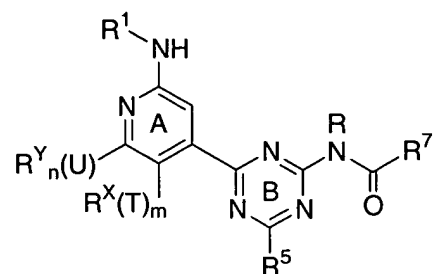
**III-A-viii**



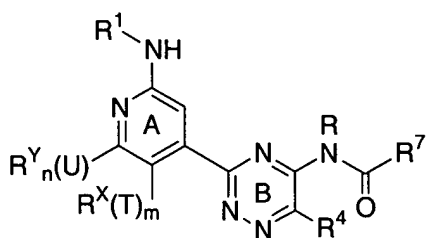
**III-A-ix**



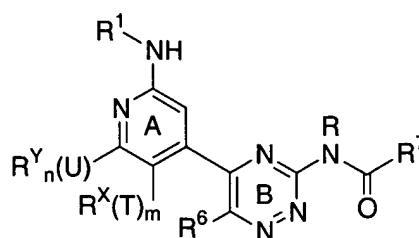
**III-A-x**



**III-A-xi**

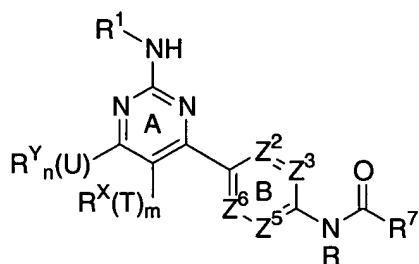


**III-A-xii**

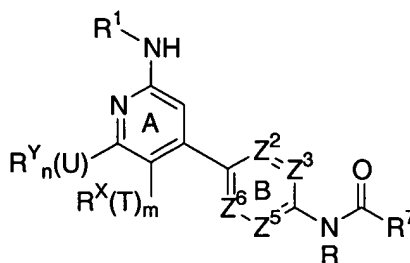


**III-A-xiii**

31. The compound of claim 1, wherein  $Z^4$  is  $CR^4$ , and  $R^4$  is  $NRC(O)R^7$ , wherein  $R^7$  is  $(CH_2)_t-$   $Y-R^8$ , wherein  $t$  is 0, 1 or 2, wherein  $Y$  is a bond or is O, S,  $NR^9$ ,  $-OCH_2-$ ,  $-SCH_2-$ ,  $-NR^9CH_2-$ ,  $O(CH_2)_2-$ ,  $-S(CH_2)_2-$ , or  $-NR^9(CH_2)_2-$ , and wherein  $R^8$  is  $Ar^2$ , or  $R^8$  and  $R^9$ , taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur, and compounds have one of formulas **II-B** or **III-B**:

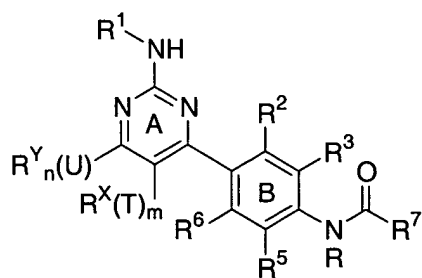


**II-B**

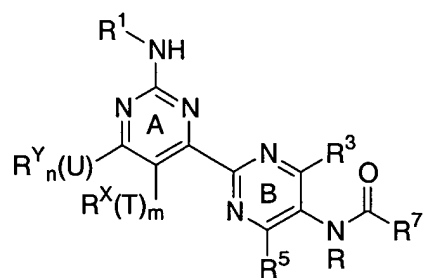


**III-B**

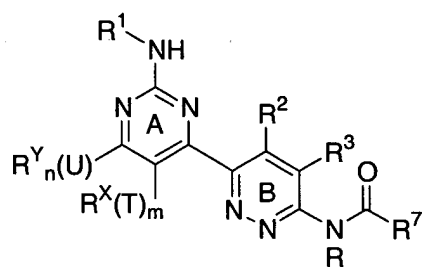
32. The compound of claim 31, wherein for compounds of formula **II-B**, ring B is selected from i, ii, iii, iv, vi, viii, ix, xii, or xiv and compounds have one of formulas **II-B-i**, **II-B-ii**, **II-B-iii**, **II-B-iv**, **II-B-vi**, **II-B-viii**, **II-B-ix**, **II-B-xii**, or **II-B-xiv**:



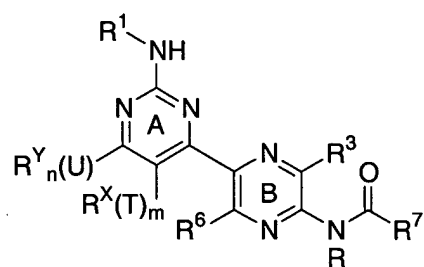
**II-B-i**



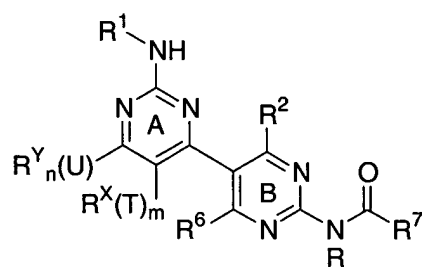
**II-B-ii**



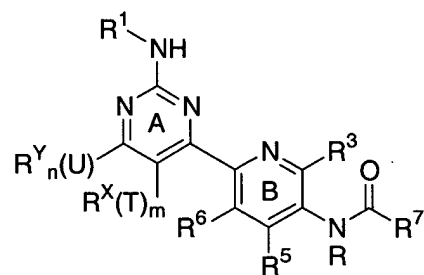
**II-B-iii**



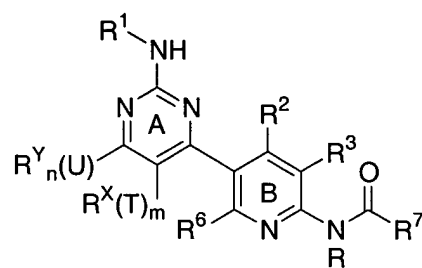
**II-B-iv**



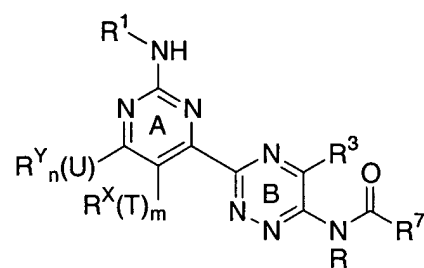
**II-B-vi**



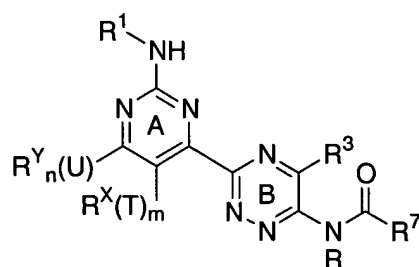
**II-B-viii**



**II-B-ix**

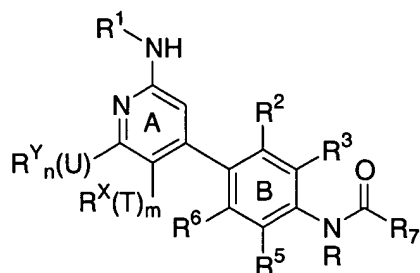


**II-B-xii**

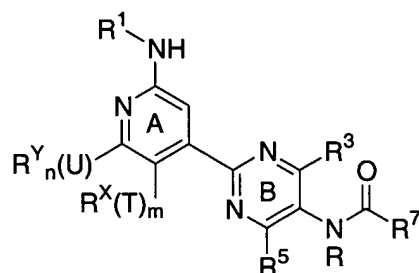


**II-B-xiv**

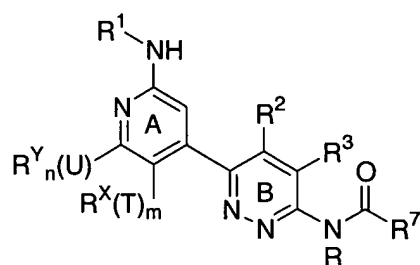
33. The compound of claim 31, wherein for compounds of formula **III-B**, ring B is selected from **i**, **ii**, **iii**, **iv**, **vi**, **viii**, **ix**, **xii**, or **xiv** and compounds have one of formulas **III-B-i**, **III-B-ii**, **III-B-iii**, **III-B-iv**, **III-B-vi**, **III-B-viii**, **III-B-ix**, **III-B-xii**, or **III-B-xiv**:



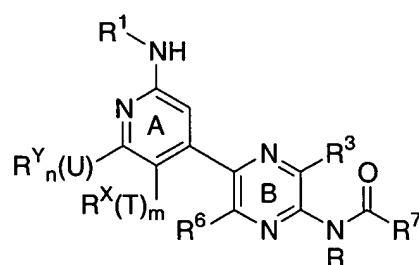
**III-B-i**



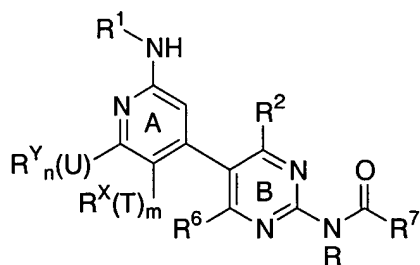
**III-B-ii**



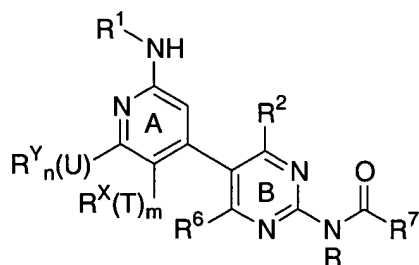
**III-B-iii**



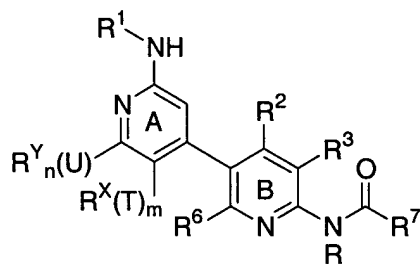
**III-B-iv**



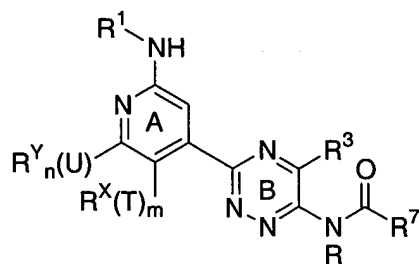
**III-B-vi**



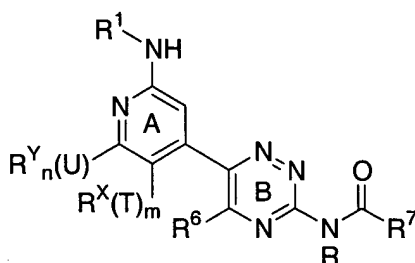
**III-B-viii**



**III-B-ix**

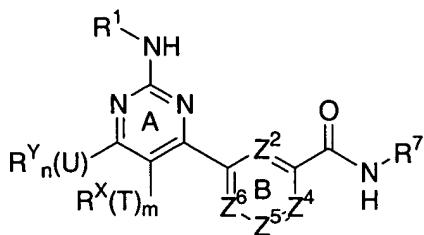


**III-B-xii**

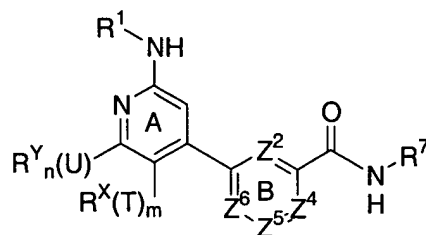


**III-B-xiv**

34. The compound of claim 1, wherein  $Z^3$  or  $Z^5$  is  $CR^3$  or  $CR^5$ , respectively, and  $R^3$  or  $R^5$  is  $C(O)N(R)(R^7)$ , wherein  $R^7$  is  $(CH_2)_t-Y-R^8$ , wherein  $t$  is 0, 1 or 2, wherein  $Y$  is a bond or is O, S,  $NR^9$ ,  $-OCH_2-$ ,  $-SCH_2-$ ,  $-NR^9CH_2$ ,  $O(CH_2)_2-$ ,  $-S(CH_2)_2-$ , or  $-NR^9(CH_2)_2$ , and wherein  $R^8$  is  $Ar^2$ , or  $R^8$  and  $R^9$ , taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur and compounds have one of formulas **II-C** or **III-C**:

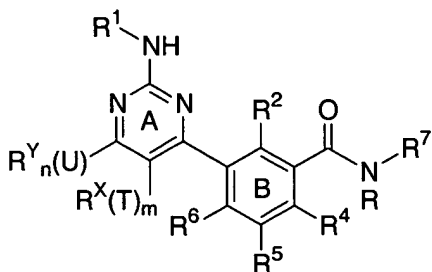


**II-C**

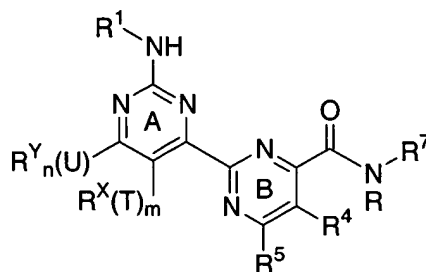


**III-C**

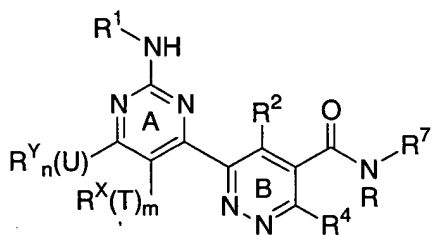
35. The compound of claim 34, wherein for compounds of formula **II-C**, ring B is selected from **i, ii, iii, iv, v, vii, viii, ix, x, xi, xii, or xiii** and compounds have one of formulas **II-C-i, II-C-ii, II-C-iii, II-C-iv, II-C-v, II-C-vii, II-C-viii, II-C-ix, II-C-x, II-C-xi, II-C-xii, or II-C-xiii**:



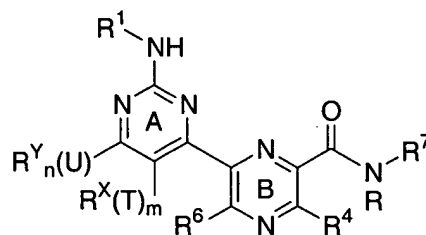
**II-C-i**



**II-C-ii**

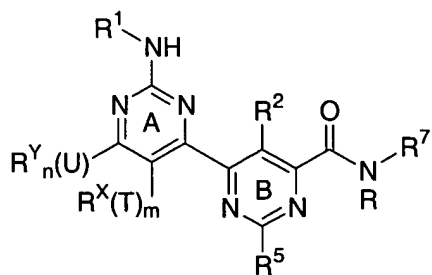


**II-C-iii**

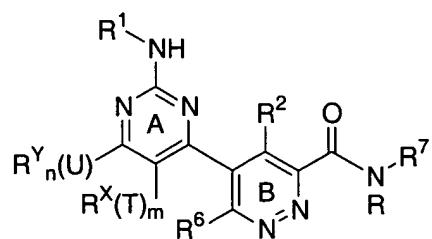


**II-C-iv**

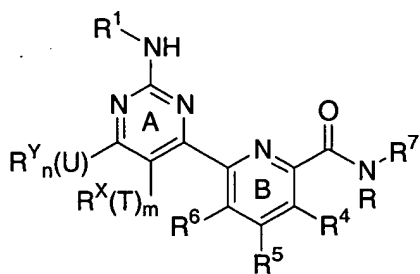




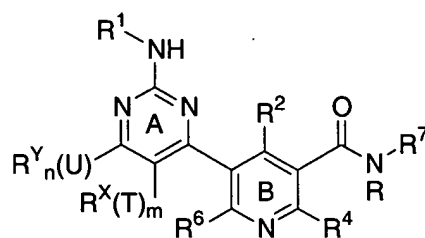
**II-C-v**



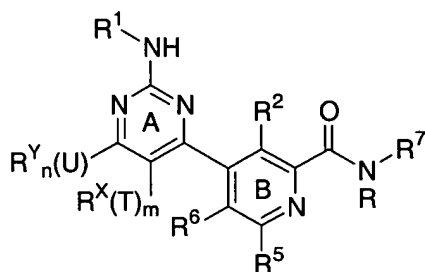
**II-C-vii**



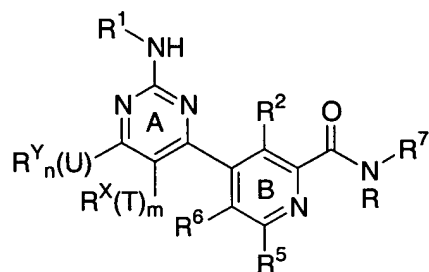
**II-C-viii**



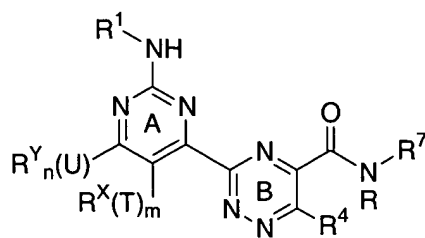
**II-C-ix**



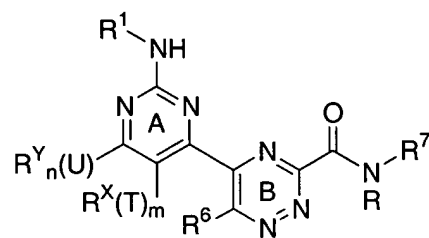
**II-C-x**



**II-C-xi**

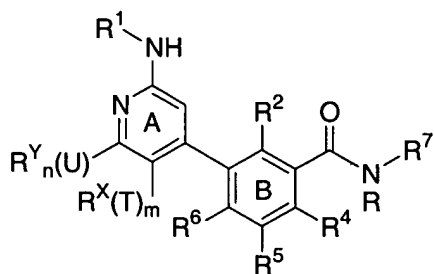


**II-C-xii**

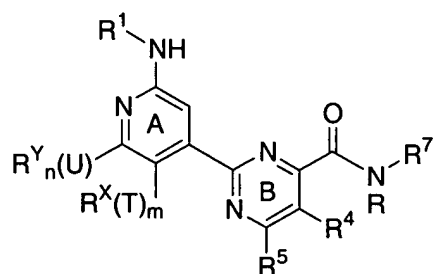


**II-C-xiii**

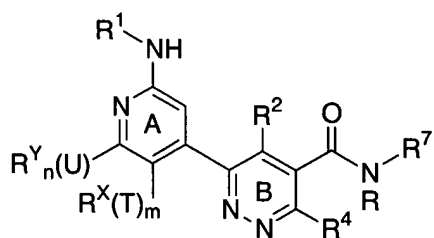
36. The compound of claim 34, wherein for compounds of formula **III-C**, ring B is selected from **i**, **ii**, **iii**, **iv**, **v**, **vii**, **viii**, **ix**, **x**, **xi**, **xii**, or **xiii** and compounds have one of formulas **III-C-i**, **III-C-ii**, **III-C-iii**, **III-C-iv**, **III-C-v**, **III-C-vii**, **III-C-viii**, **III-C-ix**, **III-C-x**, **III-C-xi**, **III-C-xii**, or **III-C-xiii** are provided as depicted below:



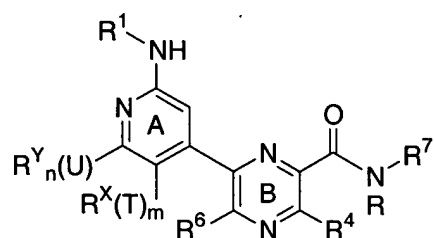
**III-C-i**



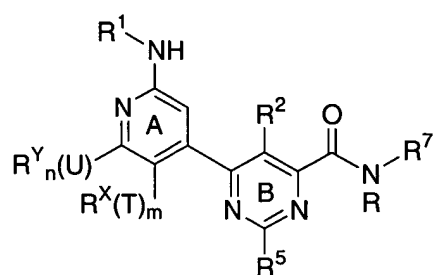
**III-C-ii**



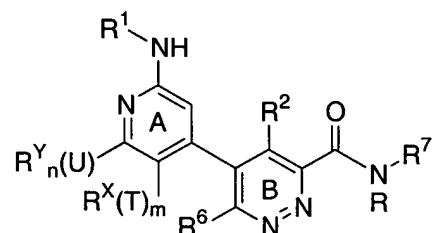
**III-C-iii**



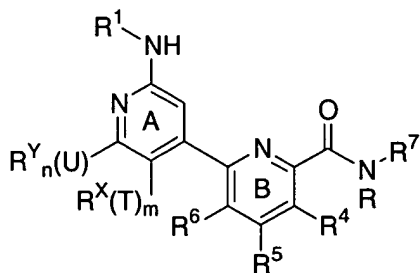
**III-C-iv**



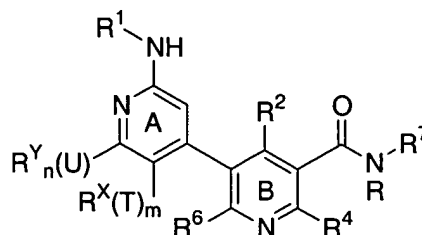
**III-C-v**



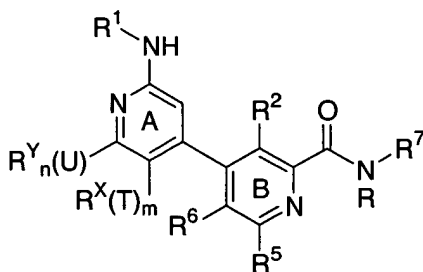
**III-C-vii**



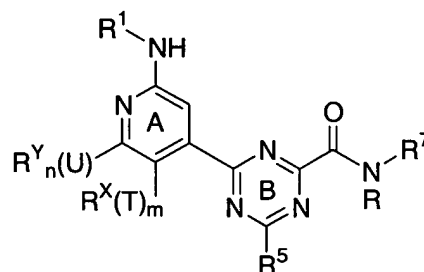
III-C-viii



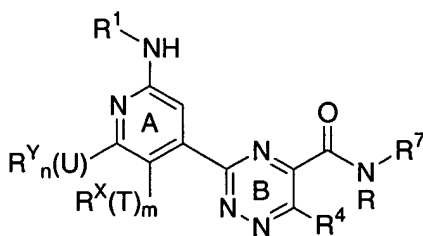
III-C-ix



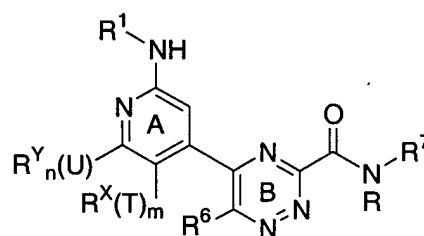
III-C-x



III-C-xi

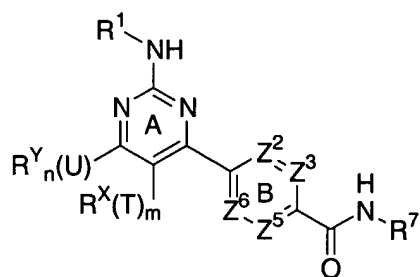


III-C-xii

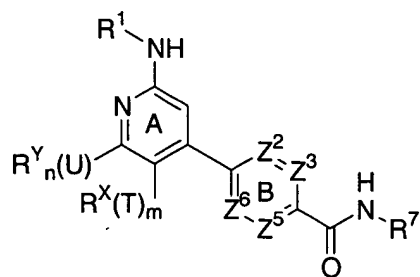


III-C-xiii

37. The compound of claim 1, wherein  $Z^4$  is  $CR^4$ , and  $R^4$  is  $C(O)N(R)(R^7)$ , wherein  $R^7$  is  $(CH_2)_t-Y-R^8$ , wherein  $t$  is 0, 1 or 2, wherein  $Y$  is a bond or is O, S,  $NR^9$ ,  $-OCH_2-$ ,  $-SCH_2-$ ,  $-NR^9CH_2$ ,  $O(CH_2)_2-$ ,  $-S(CH_2)_2$ , or  $-NR^9(CH_2)_2$ , and wherein  $R^8$  is  $Ar^2$ , or  $R^8$  and  $R^9$ , taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur and compounds have one of formulas **II-D** or **III-D**:

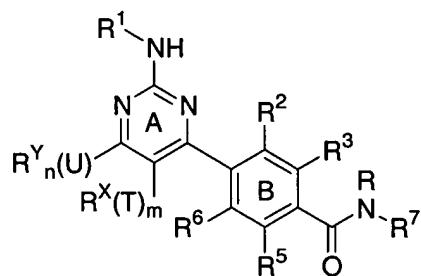


**II-D**

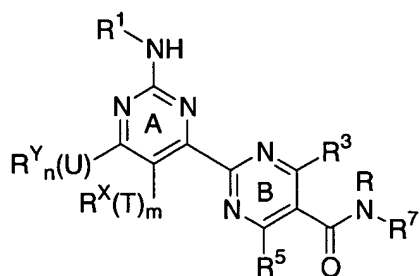


**III-D**

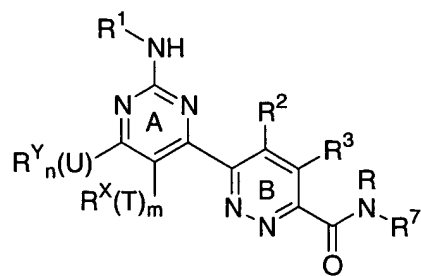
38. The compound of claim 37, wherein for compounds of formula **II-D**, ring B is selected from **i**, **ii**, **iii**, **iv**, **vi**, **viii**, **ix**, **xii**, or **xiv** and compounds have one of formulas **II-D-i**, **II-D-ii**, **II-D-iii**, **II-D-iv**, **II-D-vi**, **II-D-viii**, **II-D-ix**, **II-D-xii**, or **II-D-xiv**:



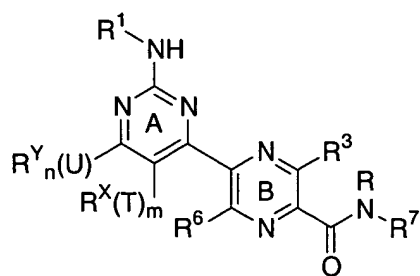
**II-D-i**



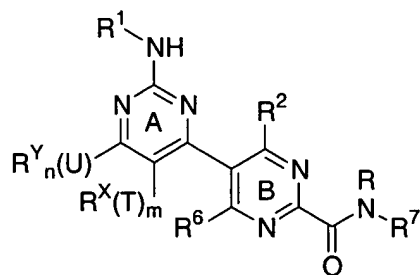
**II-D-ii**



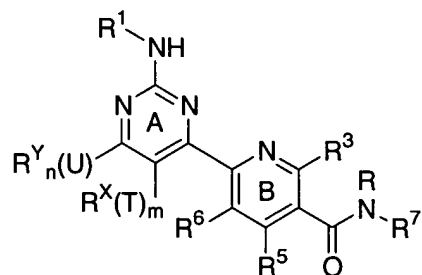
**II-D-iii**



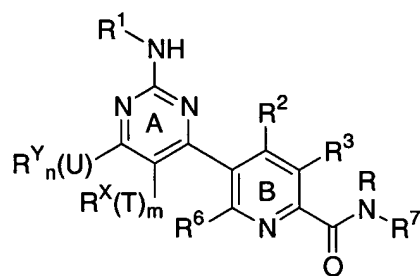
**II-D-iv**



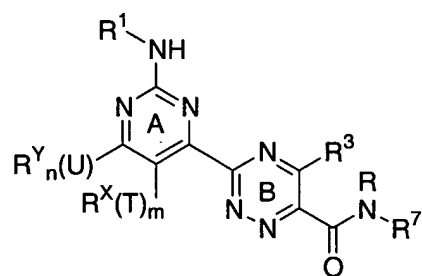
**II-D-vi**



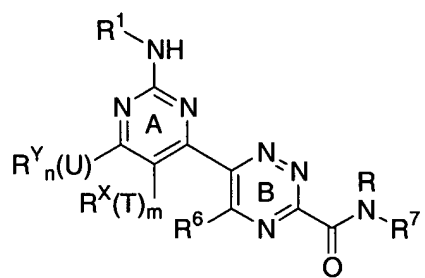
**II-D-viii**



**II-D-ix**

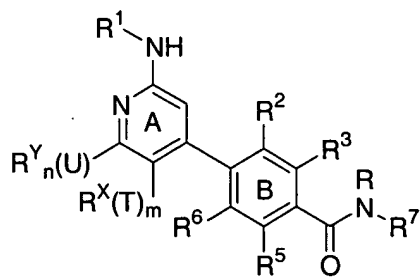


**II-D-xii**

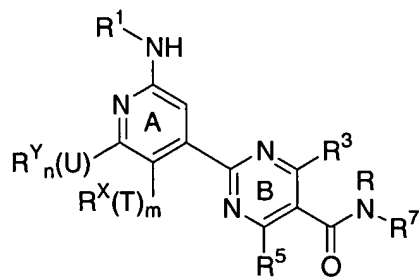


**II-D-xiv**

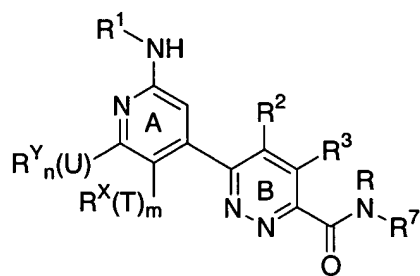
39. The compound of claim 37, wherein for compounds of formula **III-D**, ring B is selected from **i**, **ii**, **iii**, **iv**, **vi**, **viii**, **ix**, **xii**, or **xiv** and compounds have one of formulas **III-D-i**, **III-D-ii**, **III-D-iii**, **III-D-iv**, **III-D-vi**, **III-D-viii**, **III-D-ix**, **III-D-xii**, or **III-D-xiv**:



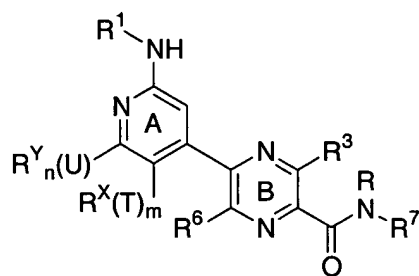
**III-D-i**



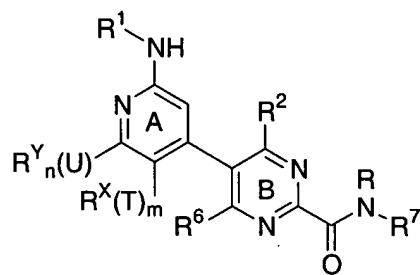
**III-D-ii**



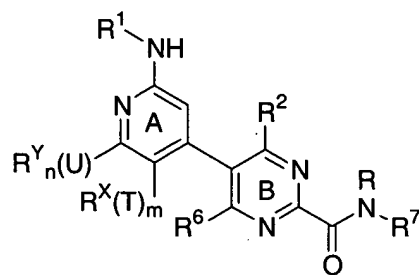
**III-D-iii**



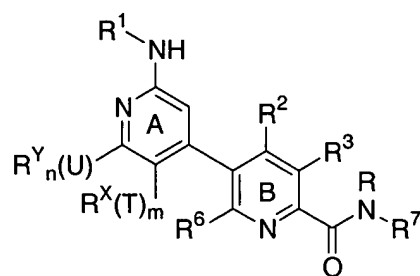
**III-D-iv**



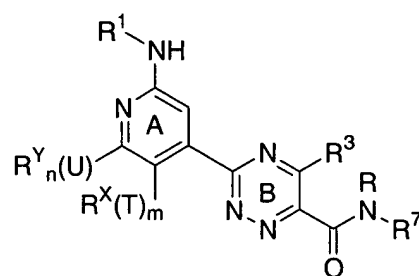
**III-D-vi**



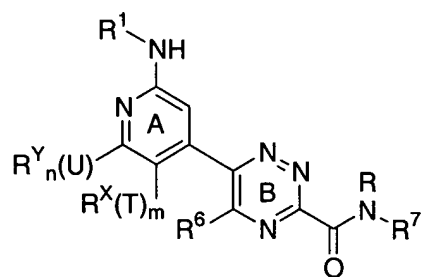
**III-D-viii**



**III-D-ix**

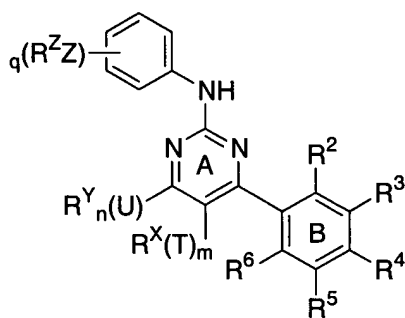


**III-D-xii**

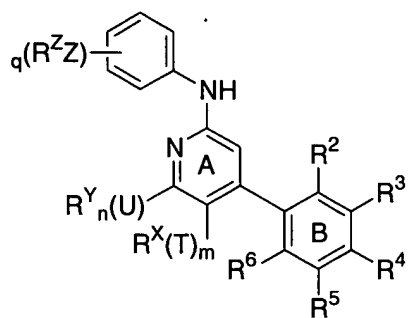


**III-D-xiv**

40. The compound of claim 1, where  $R^1$  is optionally substituted phenyl and ring B is an optionally substituted phenyl group and compounds have the general formulas **IV** or **V**:

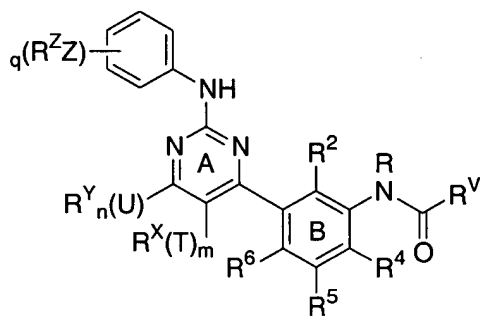


**IV**

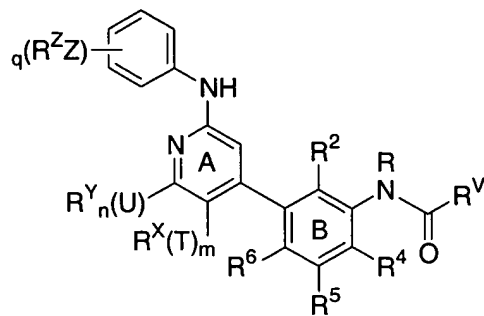


**V**

41. The compound of claim 40, wherein,  $R^3$  is  $NRCOR^7$  and compounds have the general formulae **IV-A-(i)** or **V-A-(i)**:

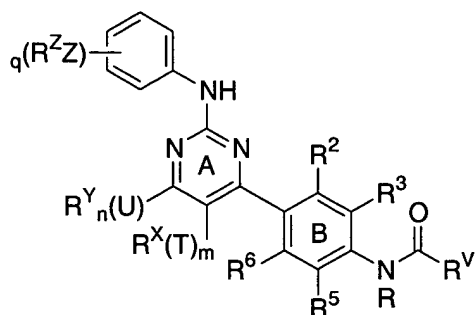


**IV-A-(i)**

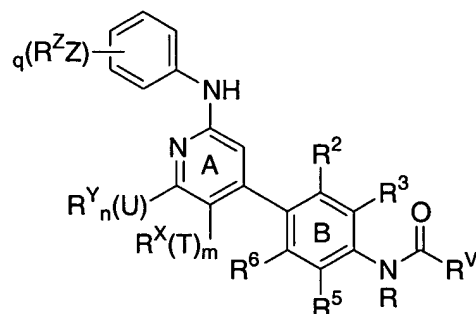


**V-A-(i)**

42. The compound of claim 40, wherein  $R^4$  is  $NRCOR^7$  and compounds have the general formulae **IV-B-(i)** or **V-B-(i)**:

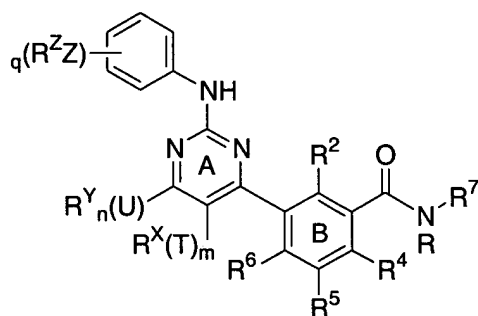


**IV-B-(i)**

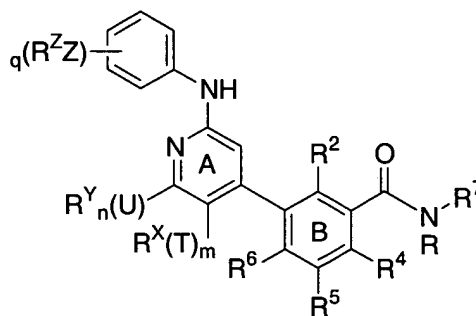


**V-B-(i)**

43. The compound of claim 40, wherein  $R^3$  is  $CONRR^7$  and compounds have the general formulae **IV-C-(i)** or **V-C-(i)**:



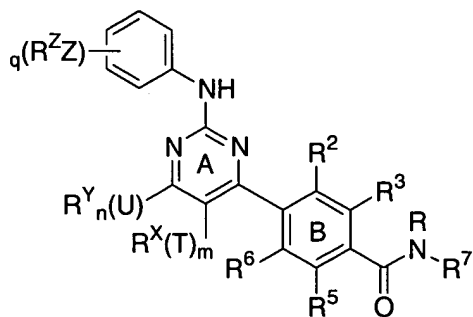
**IV-C-(i)**



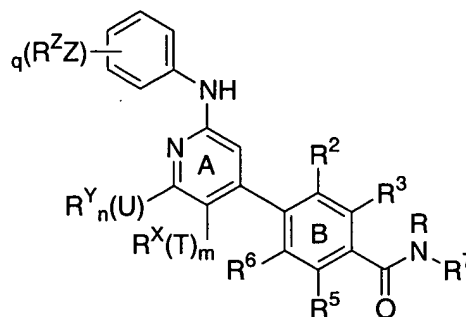
**V-C-(i)**

44. The compound of claim 40, wherein  $R^4$  is  $CONRR^7$  and compounds have the general formulae **IV-D-(i)** or **VII-D-(i)**:



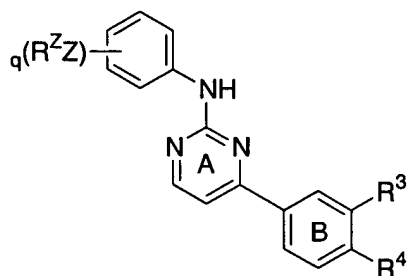


IV-D-(i)

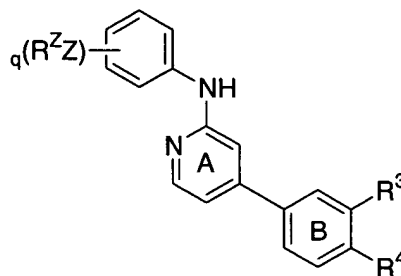


V-D-(i)

45. The compound of claim 40, wherein  $R^1$  is optionally substituted phenyl, ring A is pyrimidinyl or pyridyl, ring B is phenyl, and  $R^2$ ,  $R^5$ , and  $R^6$  are each hydrogen, and compounds have the general formulae VI and VII:



VI



VII

46. The compound of claim 40 or 45, wherein

- $q$  is 0 or 1 and  $ZR^Z$  is  $-NH_2$ ,  $-OH$ ,  $C_{1-4}$ alkoxy, or  $-SO_2NH_2$ ;
- $R^3$  is  $NRCOR^7$ , wherein  $R^7$  is  $(CH_2)_t-Y-R^8$ , and  $t$  is 0,  $Y$  is a bond, and  $R^8$  is phenyl (a), or is an optionally substituted heteroaryl moiety selected from one of groups **b** through **r**, and wherein  $r$  is 0 or 1, and  $WR^W$  substituents are halogen,  $C_{1-4}$ alkyl,  $-(R)_2$ ,  $-OR$ ,  $-SR$ ,  $-SO_2N(R)_2$ ,  $-N(R)SO_2R$ ,  $-N(R)COR$ ,  $-N(R)_2$ ,  $-CH_2OR$ ,  $-CH_2N(R)_2$ , or  $-CH_2SR$ ; and
- $R^4$  is hydrogen.

47. The compound of claim 40 or 45, wherein:

- $q$  is 0 or 1 and  $ZR^Z$  is  $-NH_2$ ,  $-OH$ ,  $C_{1-4}$ alkoxy, or  $-SO_2NH_2$ ;

- b.  $R^3$  is  $\text{CONRR}^7$ , wherein  $R^7$  is  $(\text{CH}_2)_t\text{-Y-R}^8$ , and  $t$  is 0,  $\text{Y}$  is a bond, and  $R^8$  is phenyl (a) or is an optionally substituted heteroaryl moiety selected from one of groups **b** through **r**, and wherein  $r$  is 0 or 1, and  $\text{WR}^W$  substituents are halogen,  $\text{C}_{1-4}$ alkyl,  $-(\text{R})_2$ ,  $-\text{OR}$ ,  $-\text{SR}$ ,  $-\text{SO}_2\text{N}(\text{R})_2$ ,  $-\text{N}(\text{R})\text{SO}_2\text{R}$ ,  $-\text{N}(\text{R})\text{COR}$ ,  $-\text{N}(\text{R})_2$ ,  $-\text{CH}_2\text{OR}$ ,  $-\text{CH}_2\text{N}(\text{R})_2$ , or  $-\text{CH}_2\text{SR}$ ; and
- c.  $R^4$  is hydrogen.

48. The compound of claim 40 or 45, wherein:

- a.  $q$  is 0 or 1 and  $\text{ZR}^Z$  is  $-\text{NH}_2$ ,  $-\text{OH}$ ,  $\text{C}_{1-4}$ alkoxy, or  $-\text{S}(\text{O})_2\text{NH}_2$ ;
- b.  $R^4$  is  $\text{NRCOR}^7$ , wherein  $R^7$  is  $(\text{CH}_2)_t\text{-Y-R}^8$ , and  $t$  is 0,  $\text{Y}$  is a bond, and  $R^8$  is phenyl (a) or an optionally substituted heteroaryl moiety selected from one of groups **b** through **z**, and wherein  $r$  is 0 or 1, and  $\text{WR}^W$  substituents are halogen,  $\text{C}_{1-4}$ alkyl,  $-(\text{R})_2$ ,  $-\text{OR}$ ,  $-\text{SR}$ ,  $-\text{SO}_2\text{N}(\text{R})_2$ ,  $-\text{N}(\text{R})\text{SO}_2\text{R}$ ,  $-\text{N}(\text{R})\text{COR}$ ,  $-\text{N}(\text{R})_2$ ,  $-\text{CH}_2\text{OR}$ ,  $-\text{CH}_2\text{N}(\text{R})_2$ , or  $-\text{CH}_2\text{SR}$ ; and
- c.  $R^3$  is hydrogen.

49. The compound of claim 40 or 45, wherein:

- a.  $q$  is 0 or 1 and  $\text{ZR}^Z$  is  $-\text{NH}_2$ ,  $-\text{OH}$ ,  $\text{C}_{1-4}$ alkoxy, or  $-\text{S}(\text{O})_2\text{NH}_2$ ;
- b.  $R^4$  is  $\text{CONRR}^7$ , wherein  $R^7$  is  $(\text{CH}_2)_t\text{-Y-R}^8$ , and  $t$  is 0,  $\text{Y}$  is a bond, and  $R^8$  is phenyl (a) or an optionally substituted heteroaryl moiety selected from one of groups **b** through **z**, and wherein  $r$  is 0 or 1, and  $\text{WR}^W$  substituents are halogen,  $\text{C}_{1-4}$ alkyl,  $-(\text{R})_2$ ,  $-\text{OR}$ ,  $-\text{SR}$ ,  $-\text{SO}_2\text{N}(\text{R})_2$ ,  $-\text{N}(\text{R})\text{SO}_2\text{R}$ ,  $-\text{N}(\text{R})\text{COR}$ ,  $-\text{N}(\text{R})_2$ ,  $-\text{CH}_2\text{OR}$ ,  $-\text{CH}_2\text{N}(\text{R})_2$ , or  $-\text{CH}_2\text{SR}$ ; and
- c.  $R^3$  is hydrogen.

50. The compound of claim 40 or 45, wherein:

- a.  $q$  is 0 or 1 and  $\text{ZR}^Z$  is  $-\text{NH}_2$ ,  $-\text{OH}$ ,  $\text{C}_{1-4}$ alkoxy, or  $-\text{S}(\text{O})_2\text{NH}_2$ ;
- b.  $R^3$  is  $\text{NRCOR}^7$ , wherein  $R^7$  is  $(\text{CH}_2)_t\text{-Y-R}^8$ , and  $t$  is 0 or 1,  $\text{Y}$  is  $\text{NR}^9$ , and  $R^8$  and  $R^9$ , taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein  $r$  is 0 or 1, and  $\text{WR}^W$  substituents are halogen,  $\text{C}_{1-4}$ alkyl,  $-(\text{R})_2$ ,  $-\text{OR}$ ,  $-\text{SR}$ ,  $-\text{SO}_2\text{N}(\text{R})_2$ ,  $-\text{N}(\text{R})\text{SO}_2\text{R}$ ,  $-\text{N}(\text{R})\text{COR}$ ,  $-\text{N}(\text{R})_2$ ,  $-\text{CH}_2\text{OR}$ ,  $-\text{CH}_2\text{N}(\text{R})_2$ , or  $-\text{CH}_2\text{SR}$ ; and

c.  $R^4$  is hydrogen.

51. The compound of claim 40 or 45, wherein:

- a.  $q$  is 0 or 1 and  $ZR^Z$  is  $-NH_2$ ,  $-OH$ ,  $C_{1-4}$ alkoxy, or  $-S(O)_2NH_2$ ;
- b.  $R^3$  is  $CONRR^7$ , wherein  $R^7$  is  $(CH_2)_t-Y-R^8$ , and  $t$  is 0 or 1,  $Y$  is  $NR^9$ , and  $R^8$  and  $R^9$ , taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein  $r$  is 0 or 1, and  $WR^W$  substituents are halogen,  $C_{1-4}$ alkyl,  $-(R)_2$ ,  $-OR$ ,  $-SR$ ,  $-SO_2N(R)_2$ ,  $-N(R)SO_2R$ ,  $-N(R)COR$ ,  $-N(R)_2$ ,  $-CH_2OR$ ,  $-CH_2N(R)_2$ , or  $-CH_2SR$ ; and
- c.  $R^4$  is hydrogen.

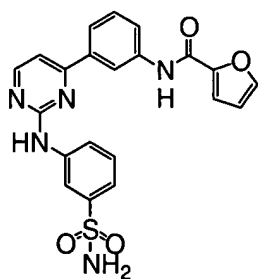
52. The compound of claim 40 or 45, wherein:

- a.  $q$  is 0 or 1 and  $ZR^Z$  is  $-NH_2$ ,  $-OH$ ,  $C_{1-4}$ alkoxy, or  $-S(O)_2NH_2$ ;
- b.  $R^4$  is  $NRCOR^7$ , wherein  $R^7$  is  $(CH_2)_t-Y-R^8$ , and  $t$  is 0 or 1,  $Y$  is  $NR^9$ , and  $R^8$  and  $R^9$ , taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein  $r$  is 0 or 1, and  $WR^W$  substituents include halogen,  $C_{1-4}$ alkyl,  $NH_2$ ,  $OH$ ,  $SH$ ,  $SO_2NH_2$ ,  $C_{1-4}$ alkoxy,  $C_{1-4}$ thioalkyl,  $CH_2OR$ ,  $CH_2N(R)_2$ , or  $CH_2SR$ ; and
- c.  $R^3$  is hydrogen.

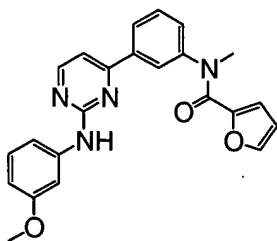
53. The compound of claim 40 or 45, wherein:

- a.  $q$  is 0 or 1 and  $ZR^Z$  is  $-NH_2$ ,  $-OH$ ,  $C_{1-4}$ alkoxy, or  $-S(O)_2NH_2$ ;
- b.  $R^4$  is  $CONRR^7$ , wherein  $R^7$  is  $(CH_2)_t-Y-R^8$ , and  $t$  is 0 or 1,  $Y$  is  $NR^9$ , and  $R^8$  and  $R^9$ , taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein  $r$  is 0 or 1, and  $WR^W$  substituents are halogen,  $C_{1-4}$ alkyl,  $-(R)_2$ ,  $-OR$ ,  $-SR$ ,  $-SO_2N(R)_2$ ,  $-N(R)SO_2R$ ,  $-N(R)COR$ ,  $-N(R)_2$ ,  $-CH_2OR$ ,  $-CH_2N(R)_2$ , or  $-CH_2SR$ ; and
- c.  $R^3$  is hydrogen.

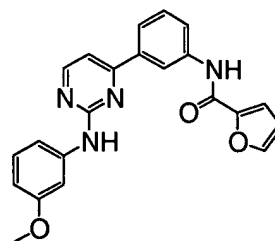
54. The compound of claim 1, having one of the following structures:



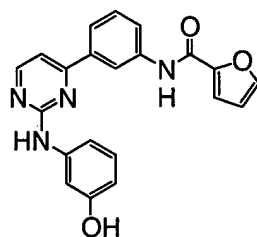
**IV-A(i)-1**



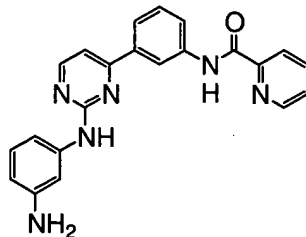
**IV-A(i)-2**



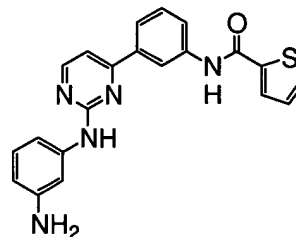
**IV-A(i)-3**



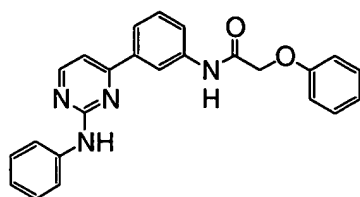
**IV-A(i)-4**



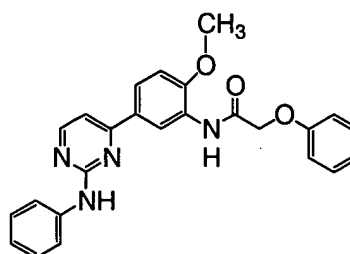
**IV-A(i)-5**



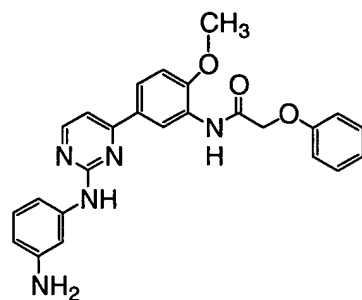
**IV-A(i)-6**



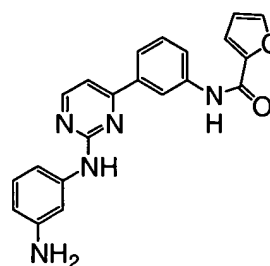
**IV-A(i)-7**



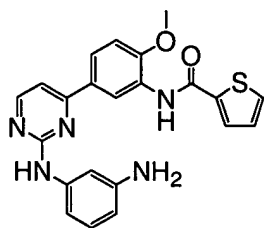
**IV-A(i)-8**



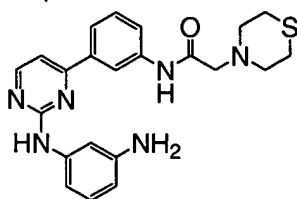
**IV-A(i)-9**



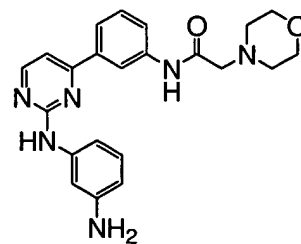
**IV-A(i)-10**



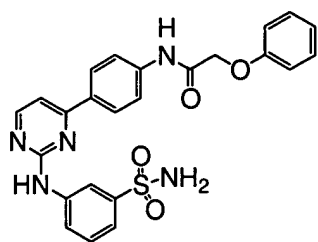
**IV-A(i)-11**



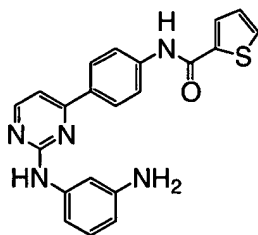
**IV-A(i)-12**



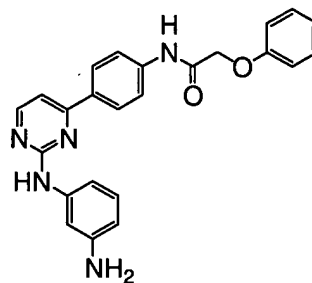
**IV-A(i)-13**



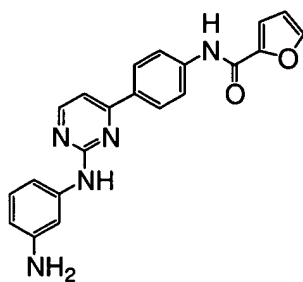
**IV-B(i)-1**



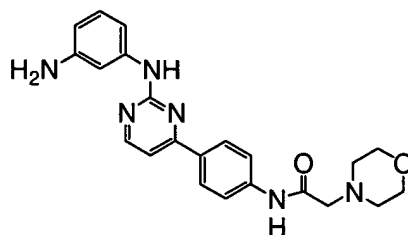
**IV-B(i)-2**



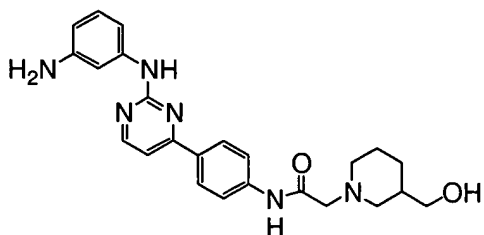
**IV-B(i)-3**



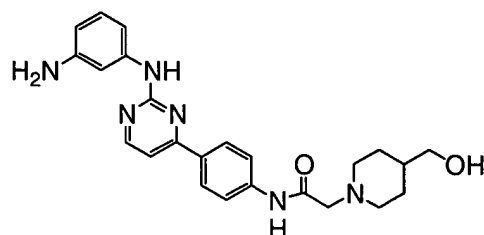
**IV-B(i)-4**



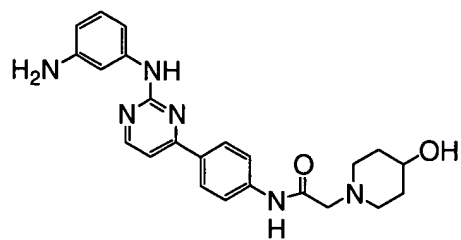
**IV-B(i)-5**



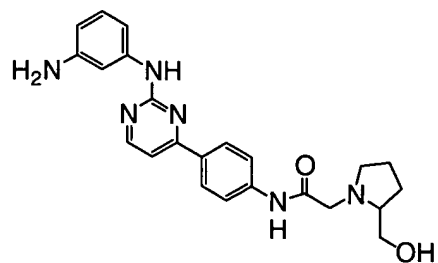
**IV-B(i)-6**



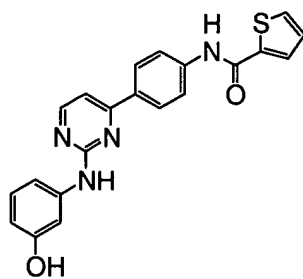
**IV-B(i)-7**



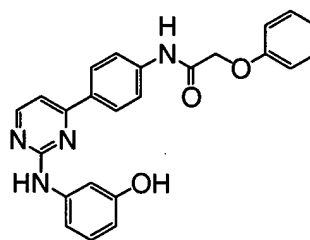
**IV-B(i)-8**



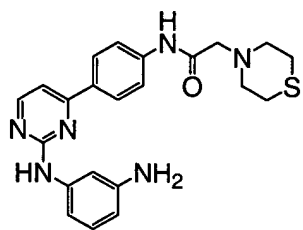
**IV-B(i)-9**



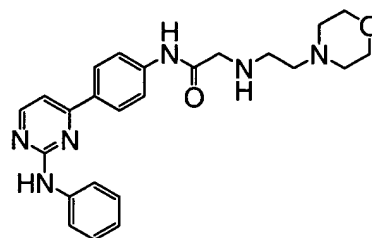
**IV-B(i)-10**



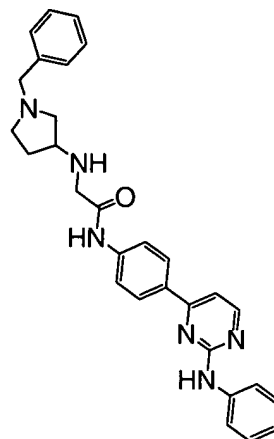
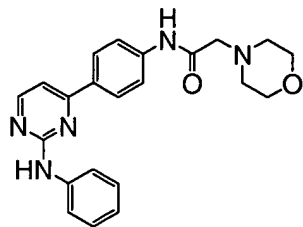
**IV-B(i)-11**



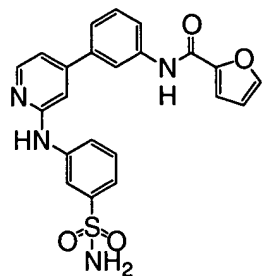
**IV-B(i)-12**



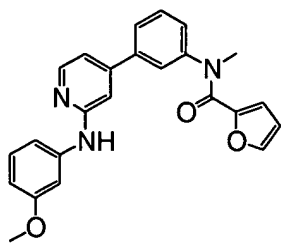
**IV-B(i)-13**



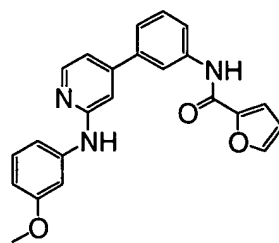
**IV-B(i)-14**



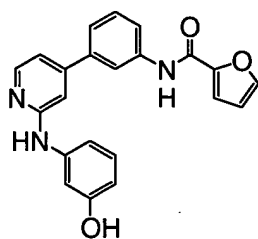
**V-A(i)-1**



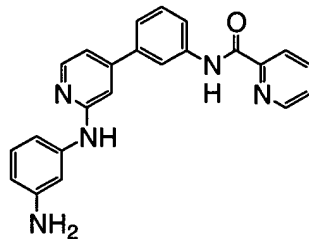
**V-A(i)-2**



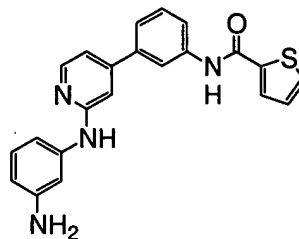
**V-A(i)-3**



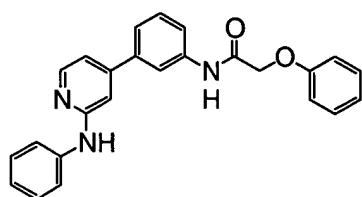
**V-A(i)-4**



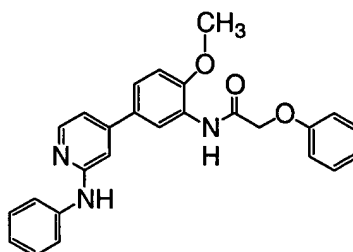
**V-A(i)-5**



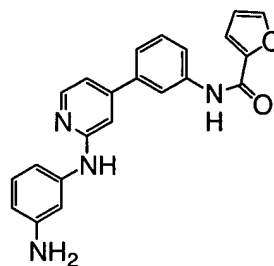
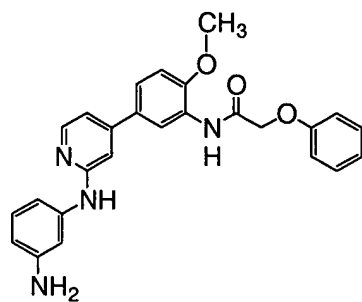
**V-A(i)-6**



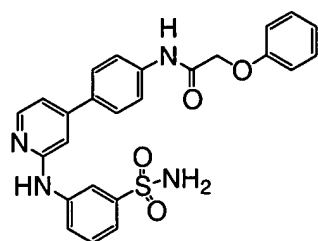
**V-A(i)-7**



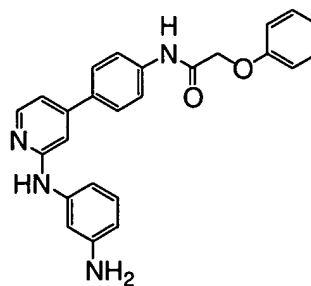
**V-A(i)-8**



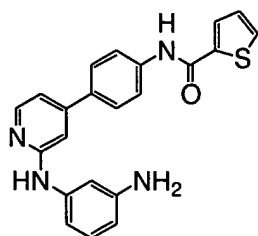
**V-A(i)-9**



**V-A(i)-10**

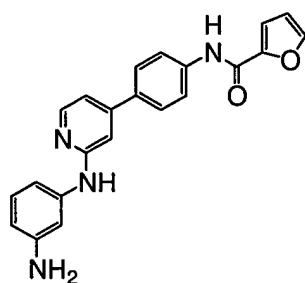


**V-B(i)-1**

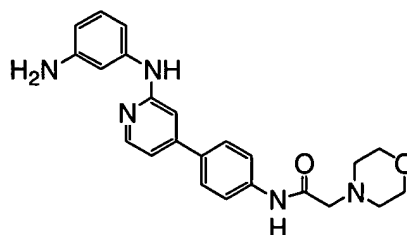


**V-B(i)-2**

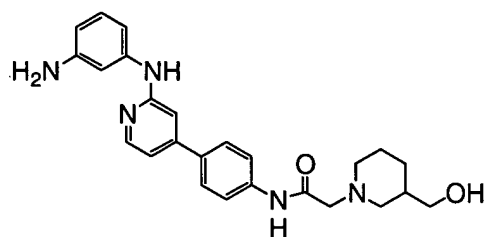
**V-B(i)-3**



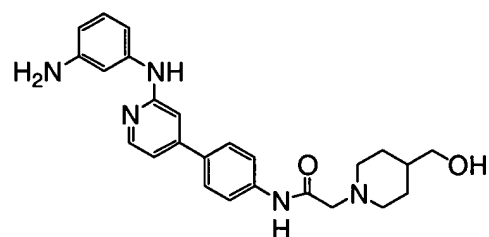
**V-B(i)-4**



**V-B(i)-5**

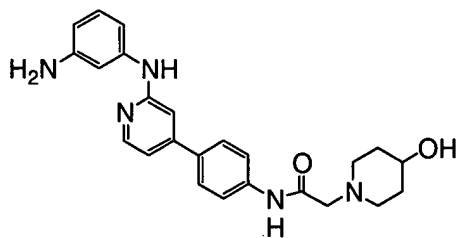


**V-B(i)-6**

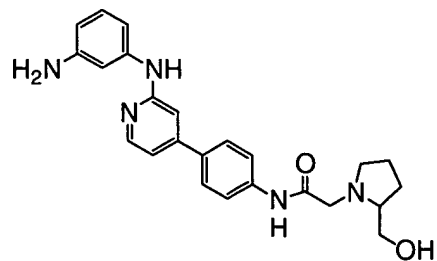


**V-B(i)-7**

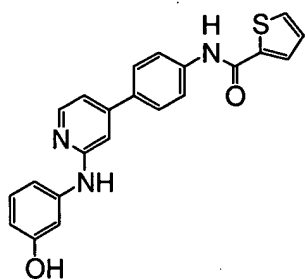




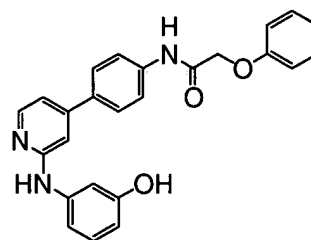
**V-B(i)-8**



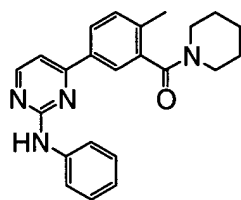
**V-B(i)-9**



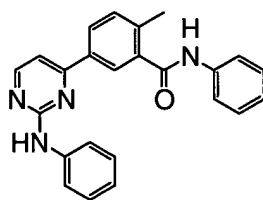
**V-B(i)-10**



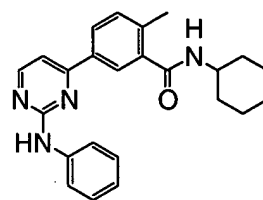
**V-B(i)-11**



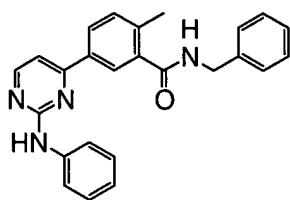
**IV-C(i)-1**



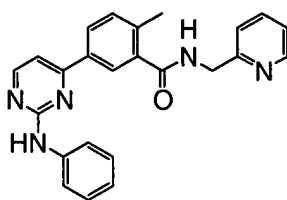
**IV-C(i)-2**



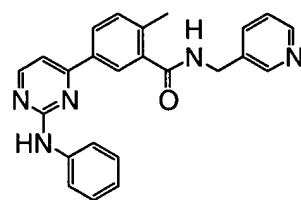
**IV-C(i)-3**



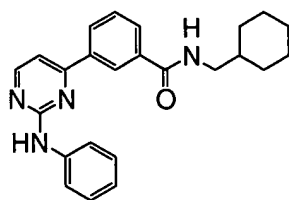
**IV-C(i)-4**



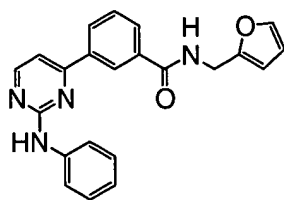
**IV-C(i)-5**



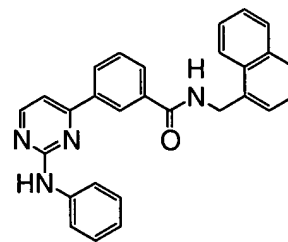
**IV-C(i)-6**



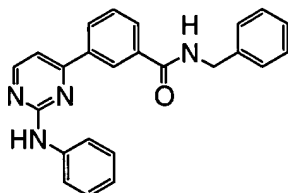
**IV-C(i)-7**



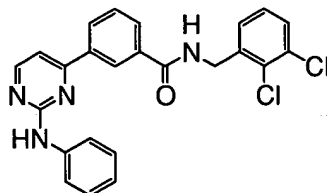
**IV-C(i)-8**



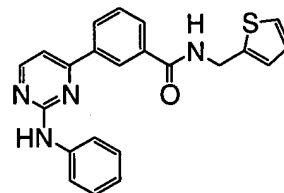
**IV-C(i)-9**



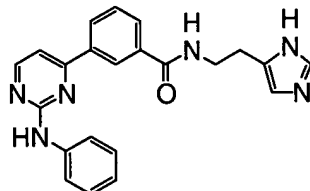
**IV-C(i)-10**



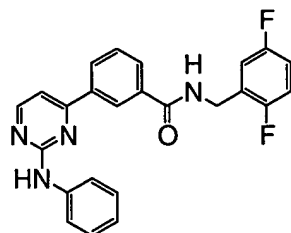
**IV-C(i)-11**



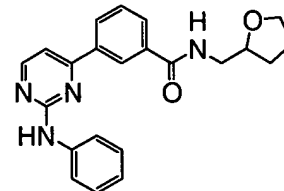
**IV-C(i)-12**



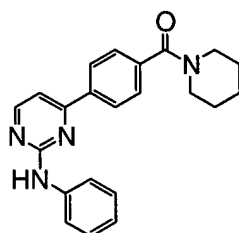
**IV-C(i)-13**



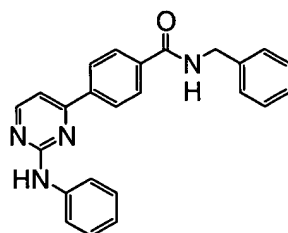
**IV-C(i)-14**



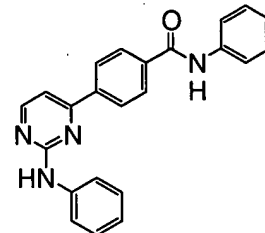
**IV-C(i)-15**



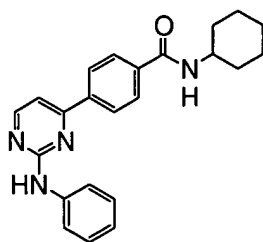
**IV-D(i)-1**



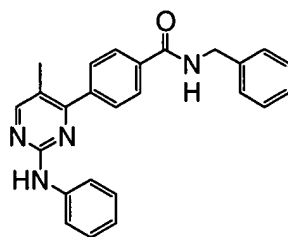
**IV-D(i)-2**



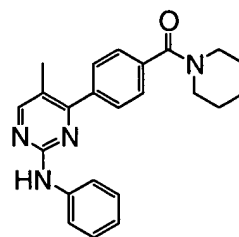
**IV-D(i)-3**



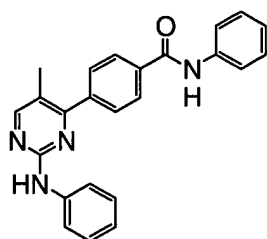
**IV-D(i)-4**



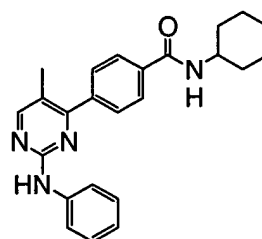
**IV-D(i)-5**



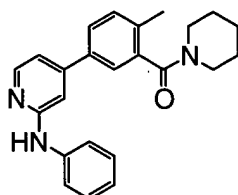
**IV-D(i)-6**



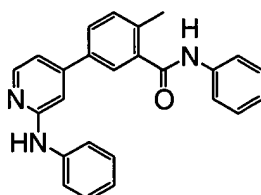
**IV-D(i)-7**



**IV-D(i)-8**



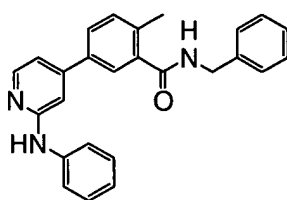
**V-C(i)-1**



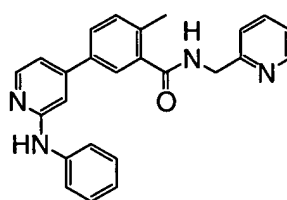
**V-C(i)-2**



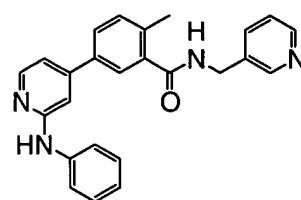
**V-C(i)-3**



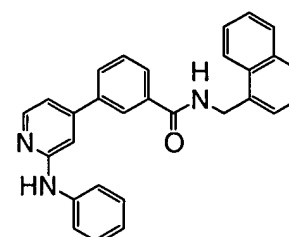
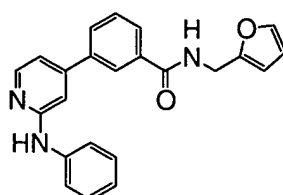
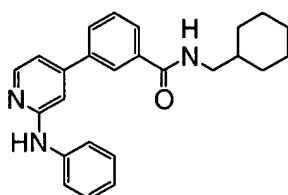
**V-C(i)-4**



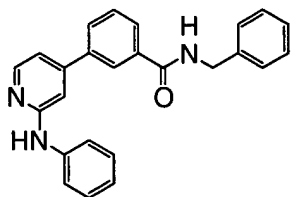
**V-C(i)-5**



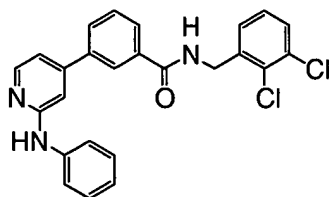
**V-C(i)-6**



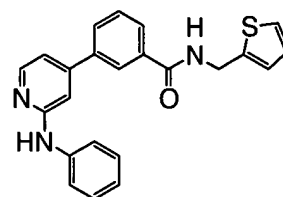
**V-C(i)-7**



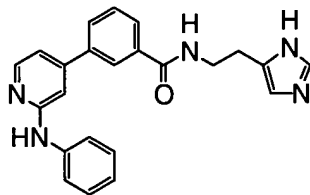
**V-C(i)-8**



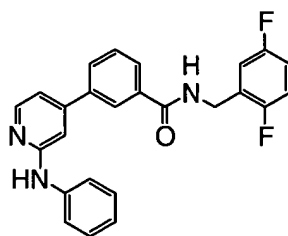
**V-C(i)-9**



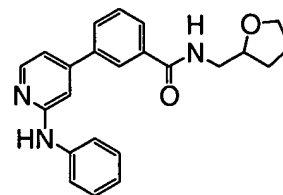
**V-C(i)-10**



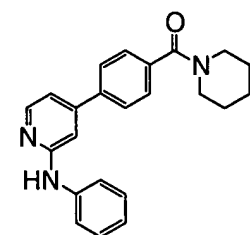
**V-C(i)-11**



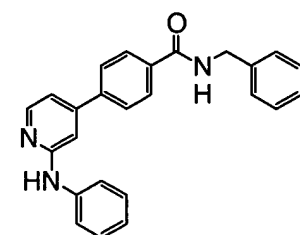
**V-C(i)-12**



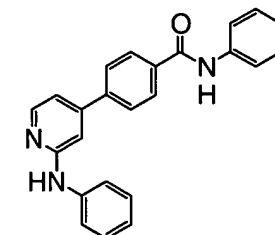
**V-C(i)-13**



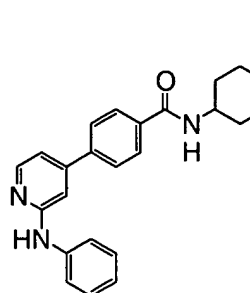
**V-C(i)-14**



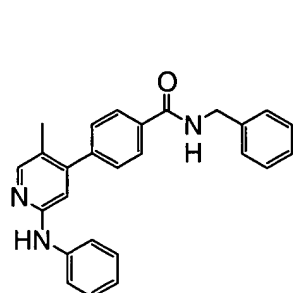
**V-C(i)-15**



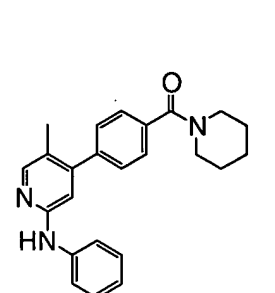
**V-D(i)-1**



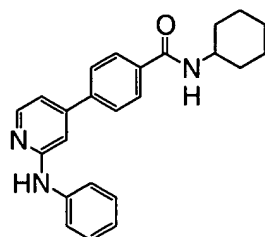
**V-D(i)-2**



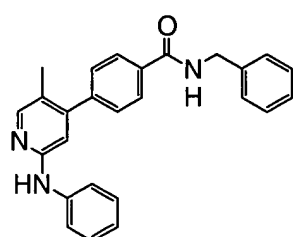
**V-D(i)-3**



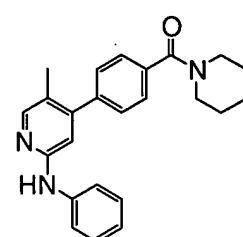
**V-D(i)-4**

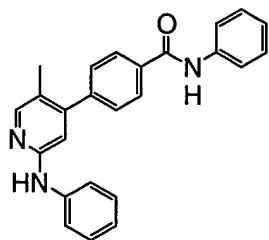


**V-D(i)-5**

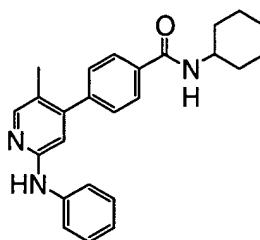


**V-D(i)-6**





**V-D(i)-7**



**V-D(i)-8**

55. A pharmaceutical composition comprising a compound according to claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

56. The composition of claim 55, further comprising an additional therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, a treatment for Alzheimer's Disease, a treatment for Parkinson's Disease, an agent for treating Multiple Sclerosis (MS), a treatment for asthma, an agent for treating schizophrenia, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an agent for treating a blood disorder, or an agent for treating an immunodeficiency disorder.

57. A method of inhibiting JAK kinase activity in a biological sample or a patient, comprising the step of contacting said biological sample or patient with:

- a) the composition of claim 55; or
- b) the compound of claim 1.

58. A method of treating or lessening the severity of a disease or disorder selected from an immune response, an autoimmune disease, a neurodegenerative disorder, or a solid or hematologic malignancy comprising administering to a patient in need thereof a compound of claim 1 or a composition of claim 55.

59. The method of claim 58, wherein the disease is an allergic or type I hypersensitivity reaction, asthma, transplant rejection, graft versus host disease, rheumatoid arthritis, amyotrophic lateral sclerosis, multiple sclerosis, Familial amyotrophic lateral sclerosis (FALS), leukemia, or lymphoma.